

U.S.S.N. 09/229,226

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AMENDMENT AND RESPONSE TO OFFICE ACTION**Clean Version of Amended Claims****Pursuant to 37 C.F.R. § 1.121(c)(1)(ii)**

1. (three times Amended) The method of claim 27 comprising
 - (a) administering acoustic energy at one or more frequencies ;
 - (b) measuring a property or the effect of the acoustic energy during the treatment with acoustic energy; and
 - (c) using the measurement obtained in step (b) to modify continued or subsequent application of acoustic energy during the treatment as needed to enhance the treatment.
2. (amended) The method of claim 1 wherein the property of the acoustic energy being measured in step b is one or more properties selected from the group consisting of pressure at one or more frequencies, and energy input at one or more frequencies.
3. (twice amended) The method of claim 1 wherein the acoustic energy is effective to alter permeability of the cells or tissues to a chemical or biological agent selected from the group consisting of peptides, proteins, sugars, polysaccharides, nucleotides, polynucleotide molecules, synthetic organic compounds, synthetic inorganic compounds, endogenous organic compounds, endogenous inorganic compounds and combinations and aggregates thereof.
4. The method of claim 3 wherein the agent is in a form selected from the group consisting of cells or virus particles, nano or microparticles, liposomes or other lipid vesicles or emulsions.
5. (amended) The method of claim 3 wherein the chemical or biological agent is delivered to cells or tissues.

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6. The method of claim 3 wherein the chemical or biological agent is detected or quantitated, further comprising
- removing biological fluid or molecules simultaneously, previously, or subsequently to the application of acoustic energy, and
- assaying the biological fluid or molecules to detect or quantitate the chemical or biological agents.
8. (amended) The method of claim 1 wherein the cells or tissues are made more permeable by the exposure to acoustic energy.
9. (twice amended) The method of claim 8 wherein the cells or tissues are made partially or completely reversibly permeable.
10. (amended) The method of claim 1 wherein the acoustic energy is applied to biological membranes.
11. (amended) The method of claim 1 wherein the tissue is skin.
12. (amended) The method of claim 1 wherein the acoustic energy is applied to cells or tissue in an amount effective to disaggregate or dissociate the cells or tissue.
13. (amended) The method of claim 1 wherein the tissues are blood vessels.
14. The method of claim 1 wherein the acoustic energy is applied at a frequency between 1 kHz and 10 MHz.
15. The method of claim 1 wherein the acoustic energy is ultrasound.
16. The method of claim 1 wherein the acoustic energy is applied at a peak positive pressure of up to 100 atmospheres.

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17. (twice amended) The method of claim 1 wherein the acoustic energy is applied under conditions to effect cavitation within or on the surface of the cells or tissues.

18. (amended) The method of claim 1 further comprising administering an agent to enhance transport within or permeability of the cells or tissues.

19. (amended) The method of claim 1 wherein the property of the acoustic energy that is measured is measured at one or more frequencies other than the frequency or frequencies at which the acoustic energy is applied.

20. (amended) The method of claim 1 wherein the property of the acoustic energy that is measured is measured at a frequency or frequencies corresponding to integer multiples of one-half or one-fourth of the frequency applied

21. (Amended) The method of claim 1 wherein the acoustic energy is measured at one or more frequencies in the acoustic spectrum which do not correspond to peaks in the acoustic spectrum and are taken from the broadband signal of the acoustic spectrum.

22. (Amended) The method of claim 19 wherein the acoustic energy measurement is analyzed using a mathematical algorithm, selected from the group consisting of Fourier Transform and Fast Fourier Transform.

23. The method of claim 1 wherein the application of the acoustic energy is modified by changing an acoustic parameter selected from the group consisting of pressure, energy, frequency, pulse length, total exposure time, duty cycle, and combinations thereof.

24. The method of claim 1 wherein the application of the acoustic energy is modified by changing a non-acoustic parameter selected from the group consisting of temperature, fluid

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gas content, administration rate of molecules to be transported, sample collection rate, device position, and combinations thereof.

25. The method of claim 1 wherein the application of the acoustic energy input is modified by interrupting the application.

26. (Three times Amended) A device comprising

(a) means for treating cells or tissue by administering acoustic energy to the cells or tissue at a first site to alter permeability, cell viability or structural integrity of cells or tissues at a second distant site;

(b) means for measuring a property or the effect of the acoustic energy during the treatment with acoustic energy; and

(c) means for using the measurement of the property of the acoustic energy to modify continued or subsequent application of acoustic energy to the cells or tissues at the first site during the treatment as needed to enhance the treatment of the cells or tissues at the second distant site.

27. (three times Amended) A method for altering transport of chemical or biological agents into or through an internal organ, internal tissue or vessel in a human or other animal using acoustic energy, comprising:

indirectly administering acoustic energy at one or more frequencies to an internal organ, internal tissue or vessel by applying a transducer to a first site on the human or other animal other than where transport is to be altered;

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wherein the acoustic energy is effective to alter transport at the internal tissue, internal organ or internal vessel.

28. (twice Amended) The method of claim 27 wherein the acoustic energy is applied to the skin or a mucosal membrane and alters transport or cell viability at an internal organ, tissue or vessel in a different tissue.

29. (Amended) The method of claim 27 wherein the acoustic energy alters transport or cell viability of tumor cells.

30. (Amended) The method of claim 27 wherein the acoustic energy alters transport into or out of the cells of molecules selected from the group consisting of therapeutic, prophylactic and diagnostic agents.

31. (twice amended) A method for altering cell viability or transport of chemical or biological agents into or through an internal organ, internal tissue or vessel in a human or other animal using acoustic energy, comprising:

indirectly administering acoustic energy at one or more frequencies to an internal organ, internal tissue or vessel by applying a transducer to a first site on the human or other animal other than where transport or cell viability is to be altered;

wherein the acoustic energy is effective to alter transport or cell viability at the internal tissue, internal organ or internal vessel, wherein the transducer is placed inside the body using invasive or minimally invasive means.

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32. (twice amended) A method for altering cell viability or transport of chemical or biological agents into or through an internal organ, internal tissue or vessel in a human or other animal using acoustic energy, comprising:

indirectly administering acoustic energy at one or more frequencies to an internal organ, internal tissue or vessel by applying a transducer to a first site on the human or other animal other than where transport or cell viability is to be altered;

wherein the acoustic energy is effective to alter transport or cell viability at the internal tissue, internal organ or internal vessel, wherein the transducer is placed within a blood vessel using a catheter.

33. (twice amended) A method for altering cell viability or transport of chemical or biological agents into or through an internal organ, internal tissue or vessel in a human or other animal using acoustic energy, comprising:

indirectly administering acoustic energy at one or more frequencies to an internal organ, internal tissue or vessel by applying a transducer to a first site on the human or other animal other than where transport or cell viability is to be altered;

wherein the acoustic energy is effective to alter transport or cell viability at the internal tissue, internal organ or internal vessel, wherein the transducer is placed within a surgical incision.

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